



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6: C12N 15/57, 9/64, 1/21, 1/19, 5/10		A3	(11) International Publication Number: WO 98/31818 (43) International Publication Date: 23 July 1998 (23.07.98)									
<p>(21) International Application Number: PCT/US98/00783</p> <p>(22) International Filing Date: 20 January 1998 (20.01.98)</p> <p>(30) Priority Data:</p> <table> <tr> <td>60/034,205</td> <td>21 January 1997 (21.01.97)</td> <td>US</td> </tr> <tr> <td>60/049,607</td> <td>13 June 1997 (13.06.97)</td> <td>US</td> </tr> <tr> <td>60/054,541</td> <td>1 August 1997 (01.08.97)</td> <td>US</td> </tr> </table> <p>(71) Applicant (for all designated States except US): HUMAN GENOME SCIENCES, INC. [US/US]; 9410 Key West Avenue, Rockville, MD 20850 (US).</p> <p>(72) Inventors; and</p> <p>(75) Inventors/Applicants (for US only): NI, Jian [CN/US]; 5502 Manorfield Road, Rockville, MD 20853 (US). RUBEN, Steven, M. [US/US]; 18528 Heritage Hills Drive, Olney, MD 20832 (US). BREWER, Laurie [US/US]; 14920 Mount Nebo Road, Poolesville, MD 20837 (US). GENTZ, Reiner [DE/US]; 13404 Fairland Park Drive, Silver Spring, MD 20904 (US). ROSEN, Craig, A. [US/US]; 22400 Rolling Hill Road, Laytonsville, MD 20882 (US).</p> <p>(74) Agents: BROOKES, A., Anders et al.; Human Genome Sciences, Inc., 9410 Key West Avenue, Rockville, MD 20850 (US).</p>		60/034,205	21 January 1997 (21.01.97)	US	60/049,607	13 June 1997 (13.06.97)	US	60/054,541	1 August 1997 (01.08.97)	US	<p>(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIGO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).</p> <p>Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i></p> <p>(88) Date of publication of the international search report: 26 November 1998 (26.11.98)</p>	
60/034,205	21 January 1997 (21.01.97)	US										
60/049,607	13 June 1997 (13.06.97)	US										
60/054,541	1 August 1997 (01.08.97)	US										
<p>(54) Title: TACE-LIKE AND MATRILYSIN-LIKE POLYPEPTIDES</p> <p>(57) Abstract</p> <p>The present invention relates to novel metalloproteinase-like proteins. In particular, isolated nucleic acid molecules are provided encoding the human TACE-like and matrilysin-like proteins. TACE-like and matrilysin-like polypeptides are also provided as are vectors, host cells and recombinant methods for producing the same. The invention further relates to screening methods for identifying agonists and antagonists of TACE-like and matrilysin-like activity. Also provided are diagnostic methods for detecting cancer and therapeutic methods for cancer and other disorders characterized by an over or under production of these metalloproteinases.</p>												
<pre> 1 ACGAGGCCCTCTGGCTGAGCCATGTTCTTCTCCCTGCCCTCTCACTGAGCTTGGAGA 60 1 M F L L I A L I T E F G R 13 61 CTGCAAGCCACAGGTTCTGAAGAAATTTCCTGCATGTACAGTTCCACCGAAGAGTT 120 14 L Q A H E G S E G I F L H V T V P R K I 33 121 AAGTCAAATGACAGTGAAGTTTCAGAGAGAAGATGTTAACATCATTAACTTGATGGA 180 34 K S N D S E V S E R K H I Y I I T I D G 53 121 CAACTTACACTCTACATCTGGAAACATCATTCTACCCAGAACCTTTGGTTAT 240 54 Q P Y T L H L G K Q S F L P Q N F L V Y 73 241 ACATAATAAATGGGATTTGCTGATTTGCTTGTGCTCCATTTTATGATGATTGGCAT 300 74 T Y N E T G S L H S V S P Y F N H H C H 93 301 TACCAAGGATATGCTGCCAATTTCAAAATTCATTGGTACACTCACTATATGTTGGT 360 94 Y Q G Y A A E F P N S F V T L S I C S G 113 361 CTCAGGGGATTTCCTCAGTTGAAAATATCAGTTATGGAATTGACCAGTAGAAATCTCA 420 114 L R G F L Q F E N I S Y G I E P V E S S 133 421 GCAAGATTGAGCATATAATTATCAAATGAAAATAATGATCCAATGATCCATTITA 480 134 A R F E H I I Y Q M K N N D P H V S I L 153 481 GCAGTAATTACAGTCATATTGGCAAAAGACCCCTACAAAAGTTCCCTAAACTCA 540 154 A V N Y S H I W O K D Q P Y K V P I N S 173 541 CAGGTGACTCTGTCATCTGATGTTACACATACTAGAACATTGCTGTGAGTTCT 600 174 Q V T V I I M * 182 601 TGTAAATCATGAAAGGAATTAGTTAGCTTGTGAGTAGGAATATTAAATTGTATT 660 661 TTCTACCTTAAATAAAACATTGAAACTTCAAAAAA 704 </pre>												

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INTERNATIONAL SEARCH REPORT

International Application No PCT/US 98/00783

A. CLASSIFICATION OF SUBJECT MATTER					
IPC 6	C12N15/57	C12N9/64	C12N1/21	C12N1/19	C12N5/10

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>EMBL/GENBANK DATABASES Accession no Y08617 Sequence identification MFTMDCIII 9 October 1996 HALL L.: "M.fascicularis mRNA for tMDC III protein" XP002069695 see the whole document</p> <p>---</p> <p>PERRY A C ET AL: "Analysis of transcripts encoding novel members of the mammalian metalloprotease-like, disintegrin-like, cysteine-rich (MDC) protein family and their expression in reproductive and non-reproductive monkey tissues." BIOCHEMICAL JOURNAL, vol. 312, 1995, pages 239-244, XP002069782 see the whole document especially figures 2 and 4</p> <p>---</p> <p>-/-</p>	1-19,40, 41
X		1-19,40, 41

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
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- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

a document member of the same patent family

Date of the actual completion of the international search

1 July 1998

Date of mailing of the international search report

08.10.98

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patenttaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl
Fax: (+31-70) 340-3016

Authorized officer

VAN DER SCHAAL C.A.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 98/00783

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	GOULD S ET AL: "Use of the DNA polymerase chain reaction for homology probing" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, vol. 86, 1989, pages 1934-1938, XP002069783 WASHINGTON US see the whole document ----	1-19, 40, 41
A	HOPP T P ET AL: "PREDICTION OF PROTEIN ANTIGENIC DETERMINANTS FROM AMINO ACID SEQUENCES" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE USA, vol. 78, no. 6, June 1981, pages 3824-3828, XP000647365 ----	9, 10, 16-19, 41
P,X	EMBL/GENBANK DATABASES Accession no AA724715, Sequence identification AA724715, 8 January 1998 HILLIER L ET AL: "WashU-NCI human EST Project" XP002069696 see the whole document ----	1-19, 40, 41
A	WOLFSBERG T G ET AL: "ADAM, A NOVEL FAMILY OF MEMBRANE PROTEINS CONTAINING A DISINTEGRIN AND METALLOPROTEASE DOMAIN: MULTIPOTENTIAL FUNCTIONS IN CELL-CELL AND CELL-MATRIX INTERACTIONS" THE JOURNAL OF CELL BIOLOGY, vol. 131, no. 2, October 1995, pages 275-278, XP002046453 ----	
A	LUNN C A ET AL: "PURIFICATION OF ADAM 10 FROM BOVINE SPLEEN AS A TNFALPHA CONVERTASE" FEBS LETTERS, vol. 400, 6 January 1997, pages 333-335, XP002046454 ----	
A	WO 96 41624 A (IMMUNEX CORP) 27 December 1996 ----	
A	GUPTA S ET AL: "Molecular cloning of the human fertilin beta subunit" BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, vol. 224, 1996, pages 318-326, XP002069699 ORLANDO, FL US -----	

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 98/00783

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:

2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see further information sheet

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-19, 40, 41

Remark on Protest

The additional search fees were accompanied by the applicant's protest.
 No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-19 40 41

A TACE-like polypeptide and nucleotides encoding the enzyme

2. Claims: 20-39 42 and 43

A matrilysin-like polypeptide and nucleotides encoding the enzyme

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 98/00783

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO 9641624 A	27-12-1996	AU 6378196 A	09-01-1997	EP 0830130 A NO 975438 A 25-03-1998 06-02-1998